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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/511,008	02/22/2000	Gregory S. Hageman	20618-000600US	3115

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TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, CA 94111-2422

EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/511,008	HAGEMAN, GREGORY S.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,21 and 68-79* is/are pending in the application.

4a) Of the above claim(s) *10,21,70-72 and 74-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,68,69,73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8/1/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed 4/6/04 have been entered. Claim 1 has been amended. Claims 1-6, 68, 69, and 73 are under current examination.

This application contains claims (10, 21, 70-72, 74-79) drawn to an invention nonelected with traverse in the reply filed on 7/16/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Election/Restrictions

Concerning the restriction requirement, Applicants reiterated the point in the last response, cited *In re Weber* case law, and insisting only a species election approach strikes a balance between unduly burden on examination and the right of an inventor. In response, the Office reiterates the response presented in pages 2-3 of the last Office action (mailed 10/6/03) maintaining that the restriction is appropriate because the Office practice is consistent with *In re Weber* case law, which requires examination of a broad generic claim. In the instant case, the generic claim of the elected invention as well as claims drawn to the elected species have been fully examined, and because the totality of the base claim has not been affected or sacrificed by the division of a single claim

into four groups of inventions, and thus the constitutional right of an inventor is properly preserved.

Applicants then assert if the Office persists in maintaining the restriction, the provision of MPEP 609 is applicable, i.e. defining claims 1-6 and 69 as linking claims. In response, linking claim practice is applicable for claims inseparable with a common technical feature, whereas Claims 1-6 and 69 are not linking claims because they could be properly divided. The distinct inventions covered by claims 1-6 and 69 appear to have a common technical feature, i.e. they all detect a protein marker in the process. However, the members of the protein groups recited in claim 1 are so unrelated and diverse that no common structure or function could be found, and a prior art reference anticipating one of the members would not render the claim obvious under 35 USC § 103 with respect to other members. This fact has been seen in prosecuting the parent of this CPA application, where the originally elected species, a protein elastin is found obvious over the prior art of record, but it does not render the other members of the recited proteins or claims as a whole obvious. Accordingly, the present restrict is proper.

Applicants further assert that since current claims are rejected only on non-prior art grounds, it is assumed that the claims in the elected group have been fully examined across their breadth with respect to each of the species within the elected group as required under MPEP 803.02, and requested continuing examination of additional species if this is not the case. In response, MPEP 803.02 requires that following species election, a Markush-type claim shall be examined *fully* with respect to the elected species and further to the extend necessary to determine the patentability. Applicants

attention is directed to MPEP § 809.02(a), which states "UPON THE ALLOWANCE OF A GENERIC CLAIM, APPLICANT WILL BE ENTITLED TO CONSIDERATION OF CLAIMS TO ADDITIONAL SPECIES WHICH ARE WRITTEN IN DEPENDENT FORM OR OTHERWISE INCLUDE ALL THE LIMITATIONS OF AN ALLOWED GENERIC CLAIM AS PROVIDED BY 37 CFR 1.141" (emphasis added). In the instant case, since no generic claim has been found allowable, no additional species is to be considered at this time.

Claim Objections

Claims 1 and 68 stand objected to for reasons of record, a complete reply to the final rejection must include cancellation of the subject matter drawn to nonelected invention or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of Claims 1-6, 68, 69, and 73 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment and response pointing to the particular section of the specification where measuring proteins in a blood sample has been contemplated.

Claims 1-6, 68, 69, and 73 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record and

following. The arguments would be addressed in the order they presented in the response.

1. With respect to whether CD1a could be detected in the blood sample, Applicants relied on the *van der Wel* and Davison college datasheet, and contend since CD1a is expressed on the surface of the dendritic cells, it can be detected in the blood. The arguments are fully considered but found not persuasive because the routine in the art for measuring proteins in the blood is measuring levels of serum or plasma protein in the absence of the cell components of the blood. This is reflected in the standard values given by any laboratory reference textbook, and the instant claim 69, wherein the recited western blot and ELISA use serum samples for blood testing. In contrast, it is noted that *van der Wel et al* use cultured cells as sample (page 3379, 1st paragraph, right column), and evaluated the CD1a expression by immunofluorescent microscope and electron microscope. *van der Wel et al* teach that CD1a is a membrane and intracellular protein, expressed abundantly on the plasma membrane and endosomes of the intracellular compartment (the paragraph bridging pages 3378-9). Accordingly, if the level of CD1a were to be measured, one would have to isolate dendritic cells and then either by direct immunohistochemical staining of the cells or extracting the CD1a protein from the cell membrane and cytoplasma for measurement. In either situation, one no longer measures the blood sample, rather a cell sample. Apparently, even though the dendritic cells may be found in a blood sample, neither the art of record nor the specification teaches that the CD1a protein marker is detectable in the serum or plasma. Further, for the sake of argument, assuming detecting protein markers in a

blood sample means measuring CD1a in dendritic cell samples, the teaching of *van der Wel* has shown that it is unlikely a measurable difference could be seen on surface expression of CD1a as cited by the previous Office action.

Applicants go on to argue that the *van der Well* article does not address CD1a expression. In response, CD1a expression is discussed in the reference and cited in the previous Office action, i.e. CD1a expression remains restricted to the plasma membrane and early endocytic tubulovescular structures during dendritic cell development, while CD1b and CD1c appear to be more active molecules acting in concert in carrying out the supposed CD1 function, and overall, CD1 cell surface expression was not detectably up-regulated during or after dendritic cell maturation, and the changes occurred in sub-cellular trafficking of CD1 molecules, (left column, page 3387)

Applicants concluded that the *van der Wel* article does not address the real issue, namely whether there is a change in CD1a levels in individuals with aneurysm and those without. In response, the argument is not impressive because the real issue should be addressed by instant specification not the art of record since it is an invention claimed by the applicants, thus, it is applicants' duty to disclose whether there is a change in CD1a levels in individuals with aneurysm and those without. Applicants are reminded that the court has stated "LAW REQUIRES THAT THE DISCLOSURE IN APPLICATION SHALL INFORM THOSE SKILLED IN THE ART HOW TO USE APPLICANT'S ALLEGED DISCOVERY, NOT HOW TO FIND OUT HOW TO USE IT FOR THEMSELVES" *In re Gardner* 166 USPQ 138 (CCPA) 1970. This case law speaks the reasoning why the Office raised the following second issue.

2. With respect to whether sufficient guidance is provided concerning the correlation of CD1a and the risk of developing aortic aneurysm, Applicants contend that one skilled in the art can readily practice the currently claimed invention without undue experimentation as directed by the claims, because variety of methods were known in the art to detect proteins in blood samples and then it simply involves comparing the value determined for two different groups.

In response, the arguments are fully considered but found not persuasive because neither the values nor risk correlations have been disclosed by the specification. Assuming the CD1a could be detected in a blood sample, the skilled artisan intending to practice the invention has to recruit proper numbers of carefully selected subjects for sample collection for both groups, which alone will not be a small job or an easy task. After the required samples are collected, one must establish a criteria or value for both groups respectively, and it is unpredictable whether the measurement would yield a difference between the two groups because the lesions of the AMD and AAA are localized whereas the dendritic cells to be tested are collected from the circulation. It is not known and the specification fails to teach whether the dendritic cells collected from the blood of a aneurysm patient differ in CD1a expression compared to that of controls, and the specification fails to establish a correlation between the CD1a levels in the blood and the risk of a subject in developing an aortic aneurysm. Accordingly, the specification fails to provide an enabling disclosure for what

is now claimed. It would have required undue experimentation for those intending to practice the invention to establish such criteria and correlation.

Applicants go on to indicate that the Examiner's concern may be primarily not all individuals that show a protein marker level that differs from that of control population will develop an aneurysm. In response, Applicant's characterization of the Examiner's concern is inaccurate. The concern is the specification only contemplates using CD1a marker as a risk indicator, however, neither the art of record nor specification teaches that the CD1a could be differentially detected in the blood of a aneurysm/macular degeneration population and a control population, nor teaches that such difference is associated with the risk for developing an aneurysm in a subject. Further, the Office cited the teachings in the art to indicate that the biological localization of CD1a is bound to cell membrane and cytosol, and is unlikely to be detected in the serum or plasma (blood sample), and it is unlikely that CD1a would be detectably different in the blood sample of the two populations, because *Van der Wel et al* (Mole Biol Cell 2003;143378-88) teach that it is the intra-cellular trafficking of CD1 isoforms not the levels of the expression that is associated with dendritic cell maturation and function. In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the references. Moreover, macular degeneration or aortic aneurysm are localized pathological alterations, neither the prior art of record nor the specification teaches how the localized change of dendritic cells correlates with the total number or maturity of dendritic cells in the circulation (blood), quantitative levels of dendritic cell markers in the biological samples, or any detectable change in diseases,

and whether techniques such as immunostaining, western blot or ELISA can sufficiently detect such change. In view of such, it is highly unpredictable or unlikely that a detectable difference of surface CD1a expression could be found in the contemplated populations. Accordingly, the specification fails to provide an enabling disclosure to teach how to assess the risk of aortic aneurysm via detecting protein markers such as CD1a in blood samples. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Applicants then assert that current method could be used as a preliminary screening tool for identifying individuals at risk in large population. In response, given the disclosure of the specification, it is unknown whether the method could be a valuable tool for large population screening for reasons set forth above.

3. Concerning selection of the control population, Applicants submitted that the subject as control can be identified in a number of different ways such as established medical procedures that detect the presence or absence of aneurysm or by historic data. In response, the issue here is that claims are drawn to a method for assessing a subject's risk for an aortic aneurysm, thus, such subject should not have shown any sign of aneurysm detectable by conventional medical procedures (otherwise it won't be necessary to make such assessment). Hence, those who have a negative finding by the conventional procedure may include subjects at risk. The specification fails to teach how to select controls so that those high-risk subjects would have minimal possibility to be included in the normal control group (otherwise the data would affect the baseline

values for the protein marker to be detected). With regard to the historic data, since no art of record nor specification provides such data, it is not available for the CD1a in blood samples. Accordingly, the specification fails to provide an enabling disclosure for what is now claimed.

For reasons of record and those set forth foregoing, the specification fails to meet the statutory enablement requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 68, 69, and 73 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants fail to address the rejection, thus the rejection stands for reasons of record.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JANICE LI
PATENT EXAMINER

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
June 25, 2004